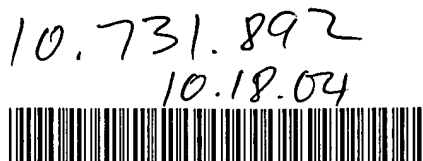


Europäisches Patentamt
European Patent Office
Office européen des brevets



(11) EP 0 998 958 A2

(12) **EUROPEAN PATENT APPLICATION**

(43) Date of publication:
10.05.2000 Bulletin 2000/19

(51) Int. Cl.⁷: A61N 1/36

(21) Application number: 99120925.5

(22) Date of filing: 02.11.1999

(84) Designated Contracting States:
AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU
MC NL PT SE
Designated Extension States:
AL LT LV MK RO SI

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(30) Priority: 05.11.1998 US 186490

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(54) **System for optimized brain stimulation**

(57) There is provided apparatus for testing to optimally place a deep brain lead 40, particularly for stimulating the GPI or other deep brain target to treat neurological disorders such as Parkinson's Disease and the like. The invention embraces determining the location of a feedback target such as the motor cortex, the location of the deep brain target, and inserting a test lead along a substantially linear trajectory so as to be able to stimulate both concurrently. The test lead has an electrode 46 at about its distal end for stimulation of the deep brain target, and an electrode 44 adjustably positioned 3-8 cm proximal for stimulation of the motor cortex. When stimulation is applied concurrently through both electrode, the affected body portion, e. g. limb, can be made to move when and if the deep brain electrode is optimally positioned. The position can be checked during surgical implant of the system, and the lead position adjusted for the permanently implanted lead can be determined during the surgical procedure.

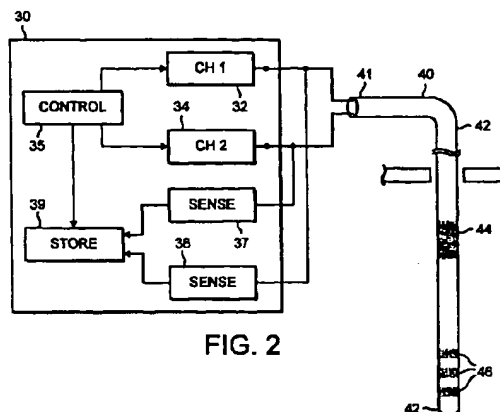


FIG. 2

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Description

[0001] This invention lies in the field of systems for brain stimulation and recording of brain activity and, more particularly, systems for placement of the lead for stimulating and/or recording at an optimized physiological brain target, for the treatment of conditions such as movement disorders.

[0002] Deep Brain Stimulation (DBS) has been found to be successful in treating a variety of brain-controlled disorders, including movement disorders. Generally, such treatment involves placement of DBS type lead through a burr hole drilled in the patient's skull, followed by placement of the lead and then applying appropriate stimulation through the lead to the physiological target. The placement portion of the treatment is very critical, and has been the subject of much attention and research. In particular, finding the deep brain target and then placing the permanent lead so that it efficiently stimulates such target is very important. See, for example, U.S. Patent Application Serial. No. 09/009,247, filed January 20, 1998, Gielen et al, which deals with the localization procedure in functional stereotactic brain surgery, i.e., the initial probing to find the optimum site for delivering the stimulation.

[0003] Finding the optimal physiological target in deep brain stimulation implants for the treatment of movement disorders is a particularly complicated task. This is especially true for the treatment of symptoms which cannot be tested at the operating table during lead implant. For instance, it is impossible to test walking and postural stability in Parkinson's Disease (PD) patients during DBS lead implant. Two other major PD symptoms, Rigidity and Akinesia, are also considered difficult to evaluate quantitatively during DBS lead implant. Thus far, no reliable quantitative evaluation procedures exist that can be performed during the surgical DBS implant procedure for these major symptoms.

[0004] A recent procedure has been suggested which allows post-operative quantitative testing of muscle function in PD. See Pascual-Leone, Rapid Rate Transcranial Magnetic Stimulation (rTMS) in Movement Disorders; Movement Disorders, Vol 11, Suppl. #1, pp.:23, 1966. In this procedure, trans-cranial magnetic stimulation of the motor cortex is used to show that the brain is able to control muscle movements in a normal way when and if the DBS electrode is implanted in the optimal physiological position in the Globus Pallidum Internae (GPi) and electrical stimulation with the appropriate parameters is applied through the DBS electrode. Thus, it was shown that those areas of the motor cortex (MC) which are involved in the control of movement in the muscle of the thumb can only be activated if the appropriate DBS stimulation is concurrently applied to the correct part of the GPi.

[0005] Based on this finding, it is reasonable that an improved procedure could be utilized for optimizing the implant position of the DBS electrode(s) in the GPi or

other neuro-modulation target for treating disorders, and particularly movement disorders, by means of deep brain stimulation. Thus, if postural instability of the patient is a major PD symptom, one might be able to find the optimal physiological target for the DBS electrode by seeing when trans-cranial magnetic stimulation of the motor cortex achieves optimal control movement of the leg muscles. However, this magnetic stimulation procedure is not suitable for intra-operative use, i.e., for testing lead position while the lead is stereotactically held. The applied very fast changing and very strong magnetic fields may interact with the DBS electrode in a comparable way as suggested for MRI imaging procedures, which is contra-indicated for DBS patients. Further, the trans-cranial magnetic stimulation coil cannot be accessed to the relevant sites of the brain when the DBS lead is being held by the stereotactic equipment. This means that the Leone procedure is not directly suggested for use in evaluating the excitability of the relevant motor cortex areas during lead implant. Thus, while the prior art procedure is appropriate for certain post-surgical testing because it is non-invasive, it is not suggested for intra-operative use.

[0006] The continued need in the art is a system and procedure that can be utilized during surgery when the DBS lead is being implanted, to determine when it has been placed in the optimal position for stimulation therapy of the patient's particular disorder, or for recording of brain activity. In general terms, the aim is a system for stimulation of the GPi or other neuro-stimulation target, and a feedback target such as the MC. A key to this invention is the recognition that during surgery, there is no need for a non-invasive way of stimulating the feedback target. The invention, rather, provides apparatus

for testing for the optimal DBS electrode position during the invasive surgery, and as part of the localization test procedure that is required in any event, enabling a reliable determination of optimal lead placement before permanent lead implant and close of surgery.

[0007] A primary object of this invention is to provide a system for determining with a test lead or permanent lead when a brain electrode is positioned optimally so during stimulation of the brain target normal patient excitability of a feedback target such as the motor cortex achieves the desired result, e.g., the desired body movement of a patient with a movement disorder. Alternatively, another object is to provide an improved capacity to record brain activity.

[0008] The invention takes advantage of the fact that during DBS lead implant, the patient's brain is already subject to an invasive procedure. This being the case, both the neuro-modulation target and the feedback target can be readily stimulated during surgery. Thus, in the case of movement disorders involving the motor cortex, the stimulation of the motor cortex concurrently with the GPi need not be limited to a non-invasive technique.

[0009] In order to achieve the above objects, the invention, according to one aspect, provides a brain stimulation system, comprising a brain stimulator or device and lead means for placement of electrodes at predetermined positions within a patient's brain, said brain stimulator device having first pulse means for generating feedback pulses for stimulating a feedback target in the patient's brain and second pulse means for generating DBS pulses for stimulating a neuro-modulation target in said patient's brain; and said lead means being connected to said device for conducting said pulses from said device to said respective targets, said lead means comprising a DBS electrode and a conductor for conducting said DBS pulses from said second pulse means to said DBS electrode, a feedback electrode and a conductor for connecting said feedback pulses from said first pulse means to said feedback electrode, and said DBS and feedback pulses from said first pulse means to said feedback electrode, and said DBS and feedback electrodes being positioned on said lead means relative to each other so that when said DBS electrode is positioned at said neuro-stimulation target said feedback electrode is positioned at said feedback target.

[0010] According to a second aspect, there is provided a lead for providing stimulation of both a feedback target in a patient's brain and a neuro-modulation target in the patient's brain, said lead also providing for recording of brain signals from either of said targets, said lead having proximal and distal ends, comprising:

- a first deep brain electrode positioned toward the distal end of said lead, and conductor means for conducting signals between said deep brain electrode and said lead proximal end; and
- a second feedback electrode positioned proximally from said deep brain electrode, and second conductor means for conducting signals between said feedback electrode and said lead proximal end.

[0011] By varying the position of the DBS electrodes, and repeatedly stimulating both the DBS target and the feedback target, and observing the relevant patient body movement or other reaction, the optimal DBS target location can be found. Also, either or both of the electrodes can be used for recording brain activity.

[0012] After the finding of the optimal DBS target location, the test lead is removed and a permanent lead positioned so that the DBS electrode(s) is located at the optimal target position. The permanent lead also preferably is aligned along the linear trajectory which includes both the neuro-modulation and the feedback targets, and carries electrodes for stimulating or recording at both targets, thereby enabling post-operative testing. The system preferably includes a generator device with dual stimulus pulse channels for providing stimuli with appropriate parameters for stimulating the respective targets, and sense channels for amplifying and process-

ing detected brain signals.

[0013] Preferred embodiments will now be described, by way of example only, with reference to the drawings.

Figure 1 is a diagrammatic view of a patient's skull and the target path or paths taken to stimulate target areas of the brain in accordance with this invention, and/or to record brain activity at the dual target sites.

Figure 2 is a schematic diagram showing a system in accordance with this invention, including an implantable stimulator/recorder device, and a test or permanent lead designed to enable dual stimulation of different brain sites and/or recording of brain signals from such sites.

Figure 3A is a diagrammatic view showing a brain stimulating lead and a slidable sleeve with a window; Figure 3B is a diagrammatic view showing the sleeve in position over the lead portion which carries electrodes for stimulating the motor cortex, thereby enabling adjustment of the location of an effective electrode on the lead for stimulating the motor cortex at the same time that the physiological brain target is stimulated.

Figure 4 is a flow diagram illustrating the primary steps taken in using the system of this invention to determine whether and when the brain lead has been optimally positioned in a patient's brain in order to treat a movement disorder or the like.

[0014] Referring now to Figure 1, there is shown a diagram of a patient's head, with burr holes BH-A and BH-B shown drilled through the patient's skull to allow entry beneath the dura. While Figure 1 presents an illustration of the specific MC/GPi embodiment, it is to be understood that the principles involved are equally applicable to other targets, as discussed above. A normal trajectory would be that indicated through the hole BH-A, along trajectory A, to the GPi. However, as indicated, the motor cortex MC is not along this line. In order to have a single one-dimensional trajectory which will involve both the GPi and the MC, burr hole BH-B is utilized, to provide a trajectory as indicated along indicated line B. It is to be noted that skull sizes vary from patient to patient, and that accordingly the distance from the GPi target and the MC target will be variable, perhaps in the range of up to 2 cm from patient to patient. For this reason, the lead of this invention preferably includes an adjustable electrode location for stimulating the feedback target, e.g., the MC, when the distal electrodes are in place for stimulating the GPi or other brain target.

[0015] Referring now to Figure 2, there is shown a diagram of a stimulator/recorder device 30 coupled to and used in connection with a lead 40. Stimulator device 30 may be, for example, a Medtronic Model 3628, or a modification thereof; and the lead may be a

modification of Medtronic InterStim Model 4300 or Medtronic DBS Lead Model 3387. As indicated, the stimulator device contains two pulse generation channels, channel 1 indicated at 32 and channel 2 at 34. Each of these channels is controlled by control block 35, which may appropriately utilize a microprocessor and/or other control and timing circuitry. The lead proximal end 41 is connected to the outputs of the device 30. Channel 1 connects to one or more lead conductors which provide electrical connection to distal electrodes indicated at 46 near the lead distal end 42. These electrodes are positioned at the neuro-modulation target, e.g., the GPi. The pulses generated by channel 1 and delivered to the deep brain location are, for example, pulses of 60-120 μ S pulse width, typically delivered at a rate in the range of about 50-250 Hz, and with a pulse amplitude of about 1-10 v. The signals delivered by channel 2 are connected through to electrode 44, which is shown positioned proximally from electrodes 46, and at a distance in the neighborhood of 3-8 cm from the distal electrodes 46, depending on the application. For example, for the MC/GPi embodiment, the positioning of electrode 44 is designed to place it proximate to the motor cortex when the distal electrodes 46 are positioned at the GPi brain target. The pulses delivered by channel 2 are, e.g., pulses of a width 1-10 ms, delivered at a rate of 1 to 5 Hz and with a voltage in the range of 1-10 v. Signals received from the electrodes are processed at sense channels 37,38 and stored at 39.

[0016] Referring now to Figures 3A and 3B, there is shown one arrangement for adjusting the position of electrode 44, to provide for stimulation of the MC concurrently with stimulation of the GPi. In this embodiment, electrode 44 is suitably comprised of a series of smaller ring electrodes, as indicated at 48, the purpose of this design being to achieve a greater lead flexibility. Alternatively, but at the cost of some flexibility, the electrode 44 may be one integral ring electrode, providing a large surface extending around the tubular body 43 of lead 40. Shown above the lead portion carrying electrode 44 is a sliding tubing, or sleeve 50, being a hollow tubing having an inner diameter adapted to just fit over the outer diameter of lead body 43. Tubing 50 is made of an electrically insulative material coating 51, except at a window portion 52 of predetermined length. The tubing 50 extends proximally a sufficient distance so that it can be manipulated, i.e., slid along the lead 43 so as to position the window portion 52 relative to the lead. In Figure 3B, the tubing is illustrated as having been slid down to register with a portion of the rings 48, providing an electrode which is adjustable along the axis of the lead by positioning of the window.

[0017] Referring now to Figure 4, there is illustrated a flow diagram of the primary steps taken in carrying out the procedure of this invention, illustrated with respect to the MC/GPi embodiment. At block 60, the test is initiated by providing a test lead as discussed in connection with Figures 2 through 3B above. Such a test lead is

provided with respective MC and GPi electrodes, where the position of the MC electrode is preferably adjustable to account for required patient variations in inter-electrode distance, as discussed in connection with Figure 1. The location of the GPi and the MC are then preliminarily determined, as indicated at 62. The approximate location of the GPi can be determined non-invasively; a more exact location of the GPi target can be determined as discussed in the above referenced U.S. Patent Application Serial No. 09/009,247. The location of the MC can be determined, e.g., by trans-cranial magnetic stimulation. With this information having been obtained, the desired one-dimensional trajectory through the two targets is known. Next, at 64, a burr hole is drilled to provide entry through the skull for the desired linear trajectory. Note that if a first burr hole is drilled in order to perform the initial localization, it can be used for placement of a separate lead to the GPi, as discussed above. Then, as indicated at 65, the test lead is stereotactically introduced along the trajectory, and the distal DBS electrode positioned in the area of the GPi. After that, at 66, the position of the MC electrode 44 is adjusted, e.g., in the manner suggested by the discussion of Figures 3A, B. The positioning of electrode 44 with respect to the MC will, of course, depend upon what body portion is to be tested or treated. After this, at 68, the two targets are stimulated, and the relevant body movement, or lack thereof, is noted. This provides the feedback for determining when the DBS electrode has been optimally located. Also, at 68, brain activity at the two sites can be recorded.

[0018] At 70, it is determined whether the DBS electrode complex 46 is optimally located. If no, which would include a state of uncertainty, the position of the DBS electrode is adjusted, as shown at 72, and then the stimulation is repeated, as indicated by the branch that loops back to 68. When the physician is satisfied that an optimal position has been found, the test is concluded, and the permanent lead is implanted, as indicated at 74. The lead is then attached to the generator device, and the patient is chronically stimulated, as indicated at 76. As mentioned above, by providing a permanent lead that also has an MC electrode, and is placed along the trajectory that encompasses both targets, subsequent tests can be conducted. Further, brain signal recordings can be obtained from the electrode sites, either concurrently, or at one site during stimulation of the other site.

[0019] There is thus provided a system for stimulating or recording at dual sites in a patient's brain, e.g., a feedback site such as the motor cortex, and a deep brain or neuro-modulation site such as the GPi. While the preferred embodiment has been presented as a single lead, either a test or permanent lead, it is to be understood that the invention can likewise be practiced by insertion of two leads, e.g., one for positioning of an electrode at the motor cortex and one for positioning of an electrode at the GPi. As used herein, the term "electrode" means either a single electrode or a plurality of

electrodes, as illustrated in Figures 2 and 3A.

Claims

1. A brain stimulation system, comprising a brain stimulator device (30) and lead means (40) for placement of electrodes at predetermined positions within a patient's brain,
 - said brain stimulator device having first pulse means (32) for generating feedback pulses for stimulating a feedback target in the patient's brain and second pulse means (34) for generating DBS pulses for stimulating a neuro-modulation target in said patient's brain; and
 - said lead means (40) being connected to said device for conducting said pulses from said device to said respective targets, said lead means comprising a DBS electrode (46) and a conductor for conducting said DBS pulses from said second pulse means to said DBS electrode, a feedback electrode (44) and a conductor for connecting said feedback pulses from said first pulse means to said feedback electrode, and said DBS and feedback pulses from said first pulse means to said feedback electrode, and said DBS and feedback electrodes being positioned on said lead means relative to each other so that when said DBS electrode is positioned at said neuro-stimulation target said feedback electrode is positioned at said feedback target.
2. The system as described in claim 1, wherein said lead means is a single lead (40), and said DBS electrode (44) is positioned near the lead distal end and said feedback electrode is positioned about 3-8 cm from said DBS electrode, whereby said lead can be inserted into the patient's brain along a predetermined path to position said electrodes at said respective feedback and neuro-modulation targets.
3. The system as described in claim 2, wherein said lead comprises adjusting means for adjusting the position of said feedback electrode to be positioned at the patient's motor cortex when said DBS electrode is positioned at said patient's GPI.
4. The system as described in claim 3, wherein said lead has a lead body, and said adjusting means comprises a slidable tubing (50) having a window (52), said tubing being slidable over said lead body to expose said feedback electrode at a desired position relative to the motor cortex.
5. The system as described in claim 4, wherein said feedback electrode has an effective surface area larger than the area of said window.
6. The system as described in any preceding claim, wherein said first pulse means comprises MC generator means for generating pulses at a rate of about 1-5 Hz for delivery to the patient's motor cortex, and parameter means for controlling said generated pulses to have a duration of about 1-10 ms and a voltage of about 1-10 Volts.
7. The system as described in any preceding claim, wherein said second pulse means comprises DBS target means for generating pulses at a rate of about 50-250 Hz, and parameter means for controlling generation of said pulses to have a duration in the range of about 60-120 μ S and a voltage in the range of about 1-10 Volts.
8. The system as described in any preceding claim, wherein said brain stimulator device further comprises means (37, 38) for receiving signals from at least one of said electrodes and means (39) for recording such signals.
9. A lead for providing stimulation of both a feedback target in a patient's brain and a neuro-modulation target in the patient's brain, said lead also providing for recording of brain signals from either of said targets, said lead having proximal and distal ends, comprising:
 - a first deep brain electrode positioned toward the distal end of said lead, and conductor means for conducting signals between said deep brain electrode and said lead proximal end; and
 - a second feedback electrode positioned proximally from said deep brain electrode, and second conductor means for conducting signals between said feedback electrode and said lead proximal end.
10. The lead as described in claim 9, wherein said feedback electrode is positioned about 3-8 cm from said deep brain electrode.
11. The lead as described in claim 9 or 10, further comprising adjusting means for adjusting the position of said feedback electrode relative to said deep brain electrode.

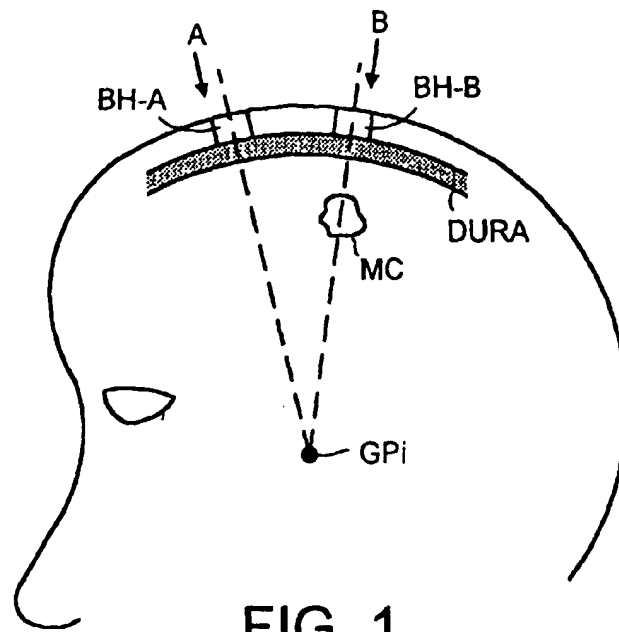


FIG. 1

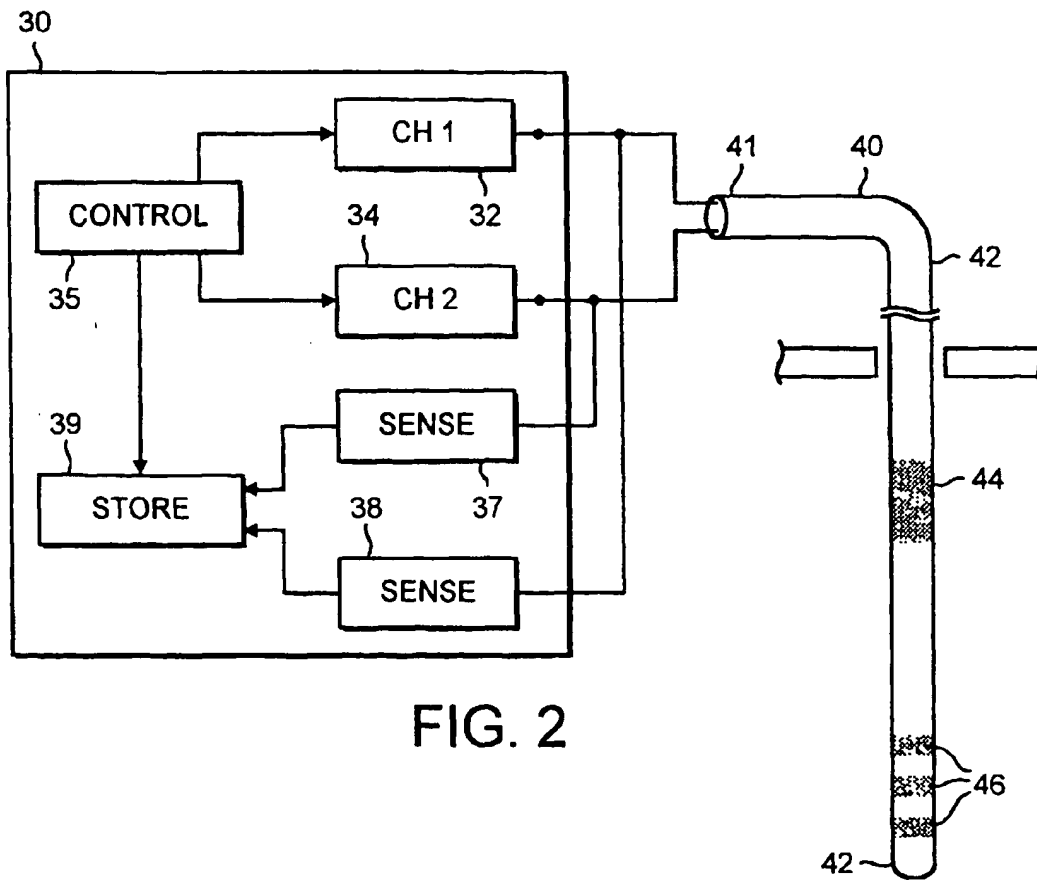


FIG. 2

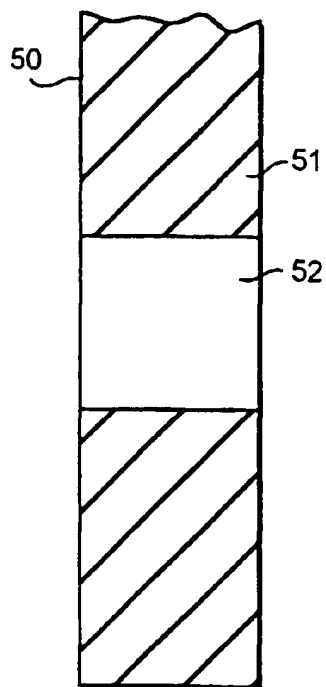


FIG. 3A

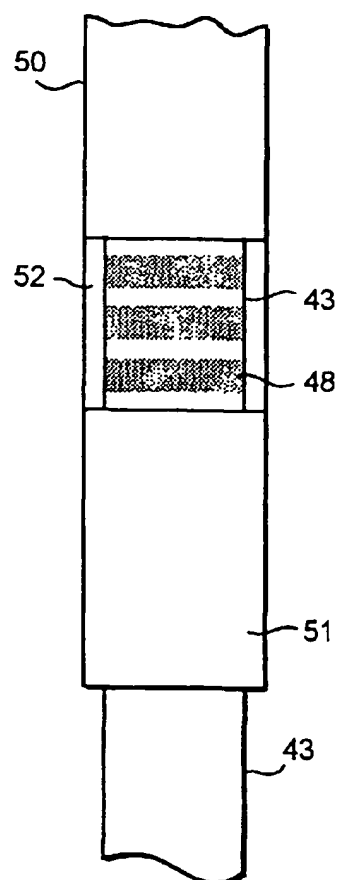
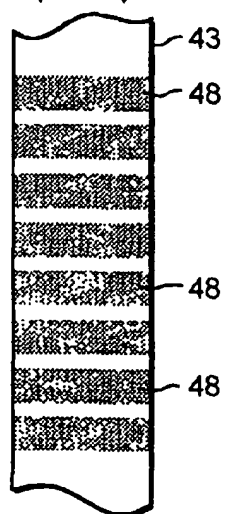


FIG. 3b

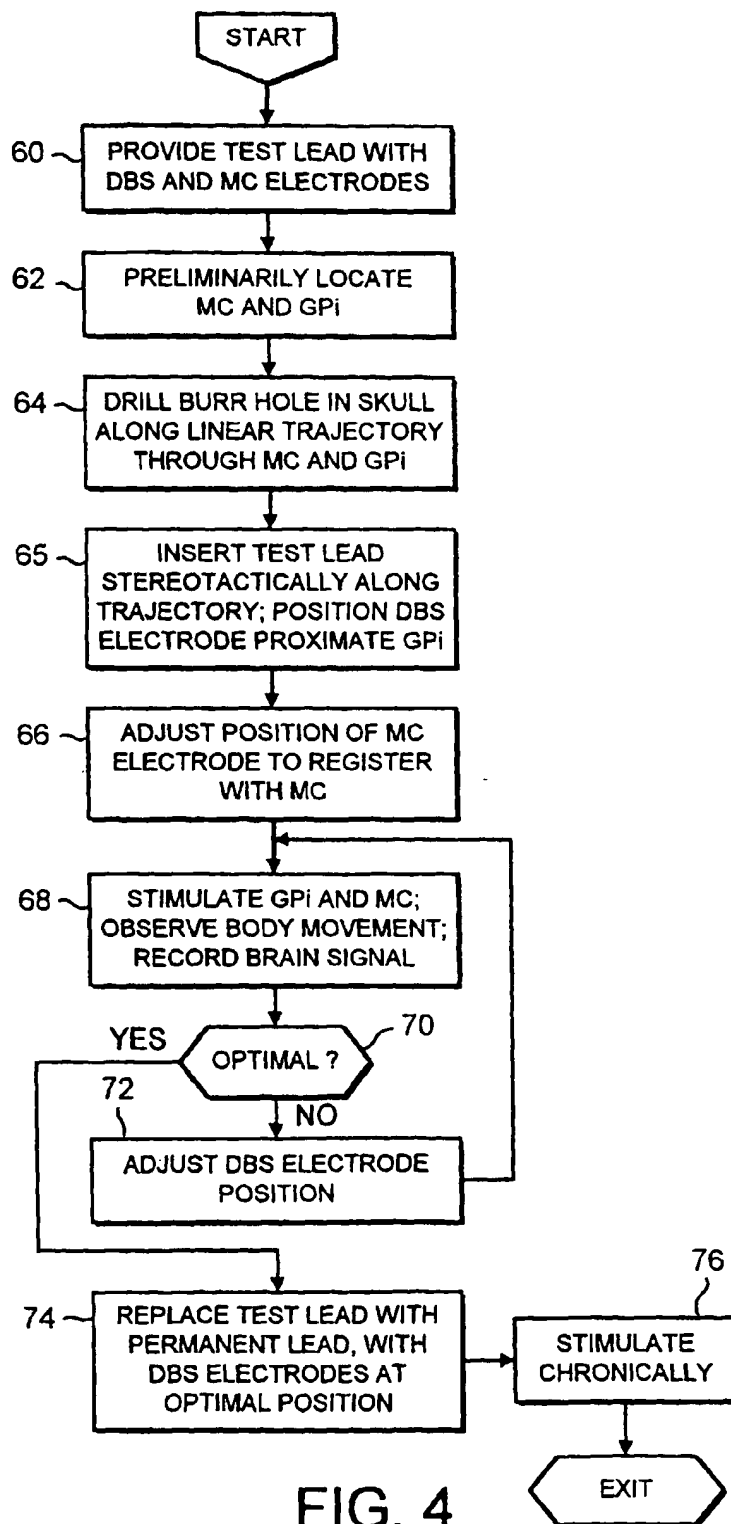


FIG. 4



(12) **EUROPEAN PATENT APPLICATION**

(88) Date of publication A3:
27.12.2000 Bulletin 2000/52

(51) Int. Cl.⁷: **A61N 1/36**

(43) Date of publication A2:
10.05.2000 Bulletin 2000/19

(21) Application number: **99120925.5**

(22) Date of filing: **02.11.1999**

(84) Designated Contracting States:
AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU
MC NL PT SE
 Designated Extension States:
AL LT LV MK RO SI

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(30) Priority: **05.11.1998 US 186490**

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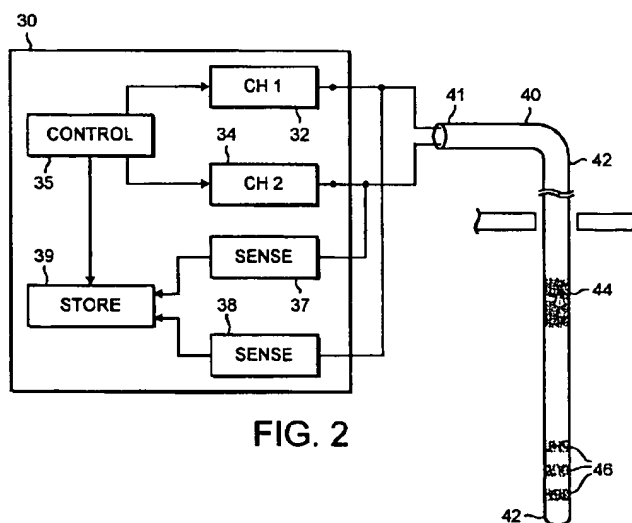


FIG. 2



European Patent
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EUROPEAN SEARCH REPORT

Application Number
EP 99 12 0925

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			A61N
The present search report has been drawn up for all claims			
Place of search		Date of completion of the search	Examiner
THE HAGUE		8 November 2000	FERRIGNO, A
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**ANNEX TO THE EUROPEAN SEARCH REPORT
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EP 99 12 0925

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
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